ABSTRACT

Different chelating agents are being used for decreasing the body burden of mercury. Data on the efficiency of such treatments in the very young are scarce and almost not available. However, young are known to be at a higher risk than adults at the same level of environmental mercury exposure. Therefore more data on the effect of chelation therapy in the very young are necessary.

We, therefore, performed experiments on albino rats of different ages by using $^{203}$Hg (as chloride from the Radiochemical Centre Amersham, England) orally or intraperitoneally. Different chelating agents - 2,3-dimercaptopropane-sulfonate-(1) (DMPS), dimercaptop- succinic acid (DMSA), zinc diethylenetriaminepentaacetate (ZnDTPA) and sodium N-(4-methoxybenzyl)-D-glucamine dithiocarbamate monohydrate (MeOBDCG) were administered as early or late treatment, orally or parenterally and their effect on the toxicokinetics of mercury in relation to age was studied. Radioactivity was determined in the whole body and organs at different time intervals after $^{203}$Hg administration.

The efficacy of the chelating agents was found to be age dependent. After parenteral administration, mercury was more easily removed from the body of older rats than of young rats. After ingestion of $^{203}$Hg, oral administration of chelating agents was found to be very efficient in reducing high gut retention in suckling rats where most of the body burden of mercury is located at this age. This treatment was efficient even after late administration.
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The efficiency of these chelating agents in relation to age, route, dose and timing of administration will also be presented. Our results indicate that all these factors should be taken into consideration to improve present methods of treatment especially in the very young.

INTRODUCTION

Chelation therapy is the treatment of choice in case of mercury intoxication (Catsch and Harmuth-Hoene, 1979). A number of chelating agents have been tested and proposed with the purpose to reduce mercury body burden. The first of these, 2,3-dimercapto-propanol (BAL), was developed more than 40 years ago (Braun et al., 1946) and has been in clinical use about 20 years in spite of its many adverse side effects. The practical usefulness of BAL is limited by a low therapeutic index (Chisolm, 1970) and increased uptake of mercury in the brain (Berlin and Ullberg, 1963). D-penicillamine is another detoxicating agent (Aposhian, 1958). By using derivatives of these agents - 2,3-dimercaptopropane-1-sulfonate, DMPS (Belonozhko, 1958), 2,3-dimercaptosuccinic acid, DMSA (Friedheim and Corvi, 1975), and N-acetyl-DL-penicillamine, NAPA (Aposhian and Aposhian, 1959) better efficacy and lower toxicity was obtained. Two water soluble derivatives of BAL, DMPS, and DMSA showed high efficacy in reducing the body burden of inorganic mercury (Gabard, 1976a; Planas-Bohne, 1981a; Wannag and Aaseth, 1980; Buchet and Lauwerys, 1989) as well as organic mercurials (Gabard, 1976b; Gabard, 1976c; Magos, 1976; Planas-Bohne, 1981b). Therapeutically, ethylenediaminetetraacetate (EDTA) is ineffective and even potentiates the toxicity of mercury (Glömmme and Gustavson, 1959) while diethylenetriamine-pentaacetate (DTPA) has poor efficacy (Nigrovic, 1963).

The usual route of mercury and chelating agent administration in most of the studies is the parenteral route. In cases of environmental exposure, the total population, including infants and young children, the oral route of mercury exposure is the expected route of its entry into the body. Also oral administration of chelation therapy would be the convenient method of treatment. Very few data are available on the efficiency of chelation treatment on oral mercury exposure.

Our earlier studies emphasized the importance of age in evaluating the efficacy of chelation therapy for several toxic metals in case of its parenteral (Pb - Jugo et al., 1975; Cd - Kostial et al., 1984a; Ce - Kargacin et al., 1983; Hg - Kostial et al., 1984b) as well as oral administration (Kostial et al., 1987a, 1987b; Kostial et al.,